

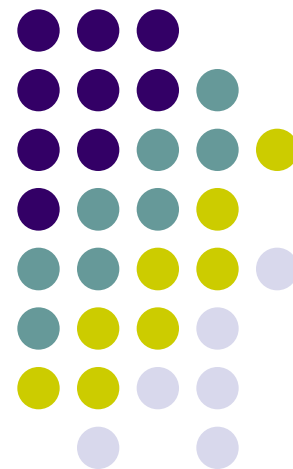
# Hypertension 2016 Journal Club



## Hussein Sheashaa, MD, FACP

Professor of Nephrology, Urology and Nephrology Center and Director of Medical E-Learning  
Unit, Mansoura University, and Executive Director of ESNT- Virtual Academy:

<http://lms.mans.edu.eg/esnt/>



**DNG August 18<sup>th</sup>, 2016**

# Corners

1. **Definitions**
2. **Goal and target of BP control**
3. **Transporters and BP**
4. **Immunity, transplantation and HTN**
5. **Obesity and HTN**
6. **Pregnancy and HTN**
7. **Adherence**
8. **Miscellaneous**

# Definitions

## Masked Hypertension and Elevated Nighttime Blood Pressure in CKD: Prevalence and Association with Target Organ Damage

All Participants (N=1492)	Controlled Clinic and ABP (n=735), 49.3%	White-Coat Hypertension (n=61), 4.1%	Masked Hypertension (n=415), 27.8%	Sustained Hypertension (n=281), 18.8%
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- Controlled BP: clinic BP <140/90 mmHg and 24-hour ABP <130/80 mmHg
- White-coat hypertension: clinic BP  $\geq$ 140/90 mmHg and 24-hour ABP <130/80 mmHg
- Masked hypertension: clinic BP <140/90 mmHg and 24-hour ABP  $\geq$ 130/80 mmHg
- Sustained hypertension: clinic BP  $\geq$ 140/90 mmHg and 24-hour ABP  $\geq$ 130/80 mmHg.

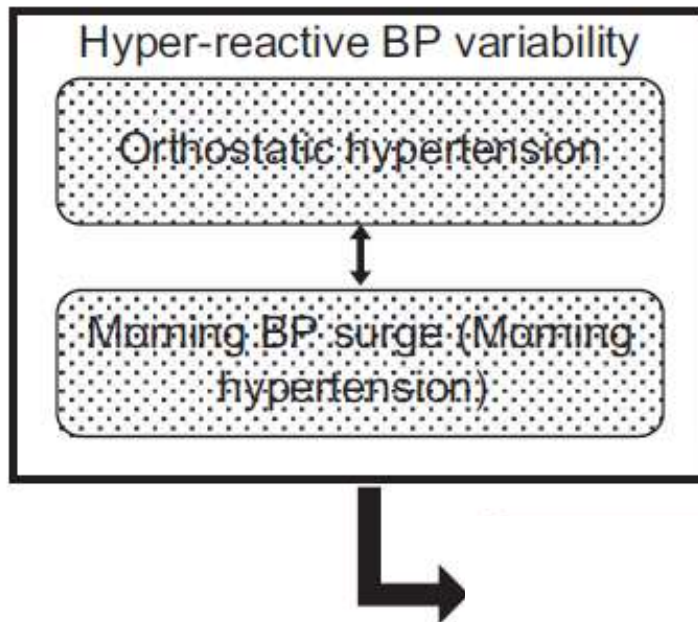
# Definitions



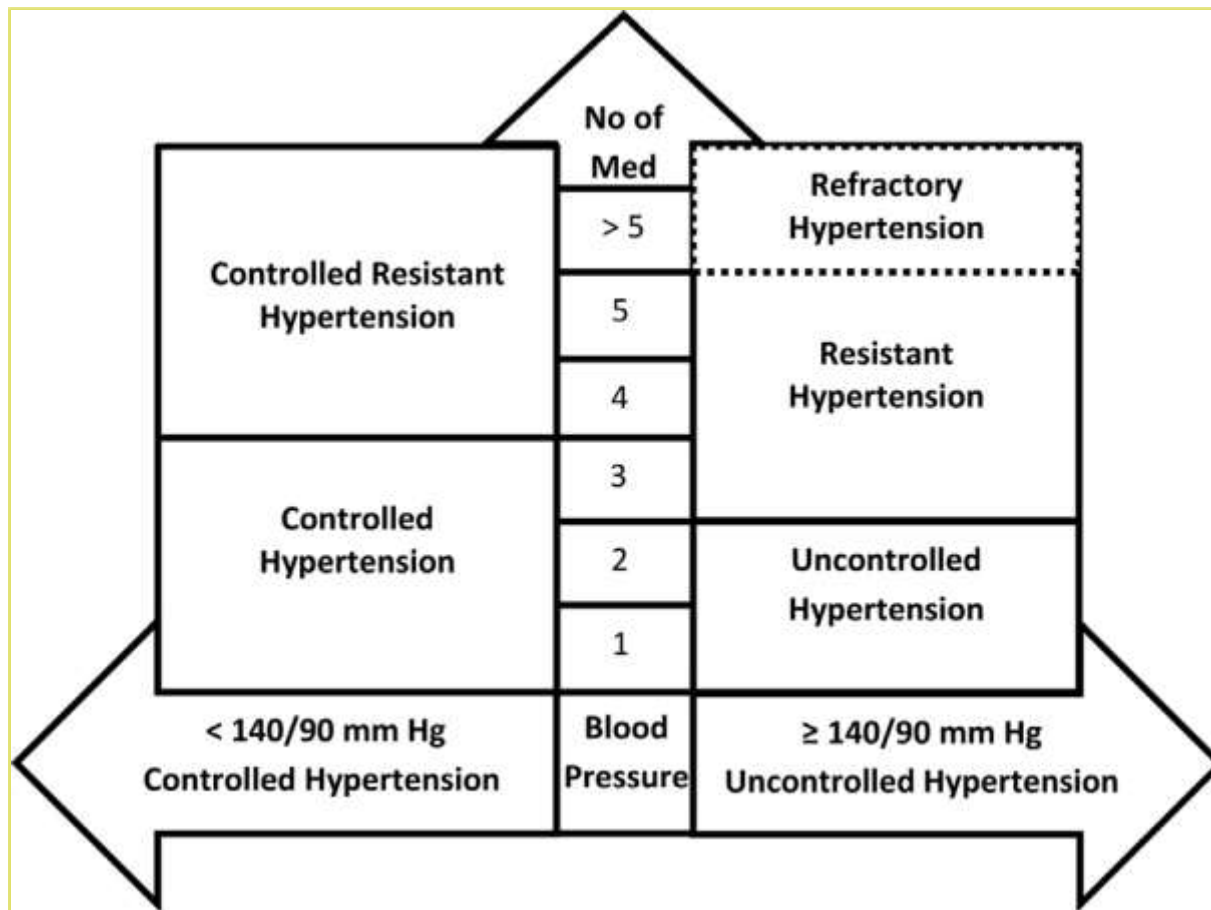
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# Definitions



# Corners

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# Hypertension Guidelines: Goal and Target

## HYPERTENSION

When should we treat  
hypertension in patients  
with diabetes?

*Sverre E. Kjeldsen and Ingrid Os*

### BP-lowering therapy and diabetes

Baseline systolic BP	Effects of BP-lowering treatment
>150 mmHg	↓ All-cause mortality ↓ Cardiovascular mortality ↓ Myocardial infarction ↓ End-stage renal disease

NATURE REVIEWS | **CARDIOLOGY** 2016

Brunström, M. & Carlberg, B. Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses. *BMJ* 352, i717 (2016).



# Management of HTN: Goal and Target

## **hypertension**

### **Clinical trials of intensive versus less intensive control of hypertension: HOPE or HYPE?**



Christina M. Wyatt<sup>1</sup> and Glenn M. Chertow<sup>2</sup>

**The recently published Heart Outcomes Prevention Evaluation trial (HOPE-3) demonstrated no benefit of lowering blood pressure with candesartan and hydrochlorothiazide in persons at intermediate cardiovascular risk and with adequate blood pressure control as determined by the enrolling physician. The results of Systolic Blood Pressure Intervention Trial (SPRINT) and HOPE-3 highlight the importance of considering differences in study design and patient population when interpreting the results of clinical trials.**

**Refers to:** Lonn EM, Bosch J, Lopez-Jaramillo P, et al. HOPE-3 Investigators. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. *N Engl J Med*. 2016;374:2009–2020.

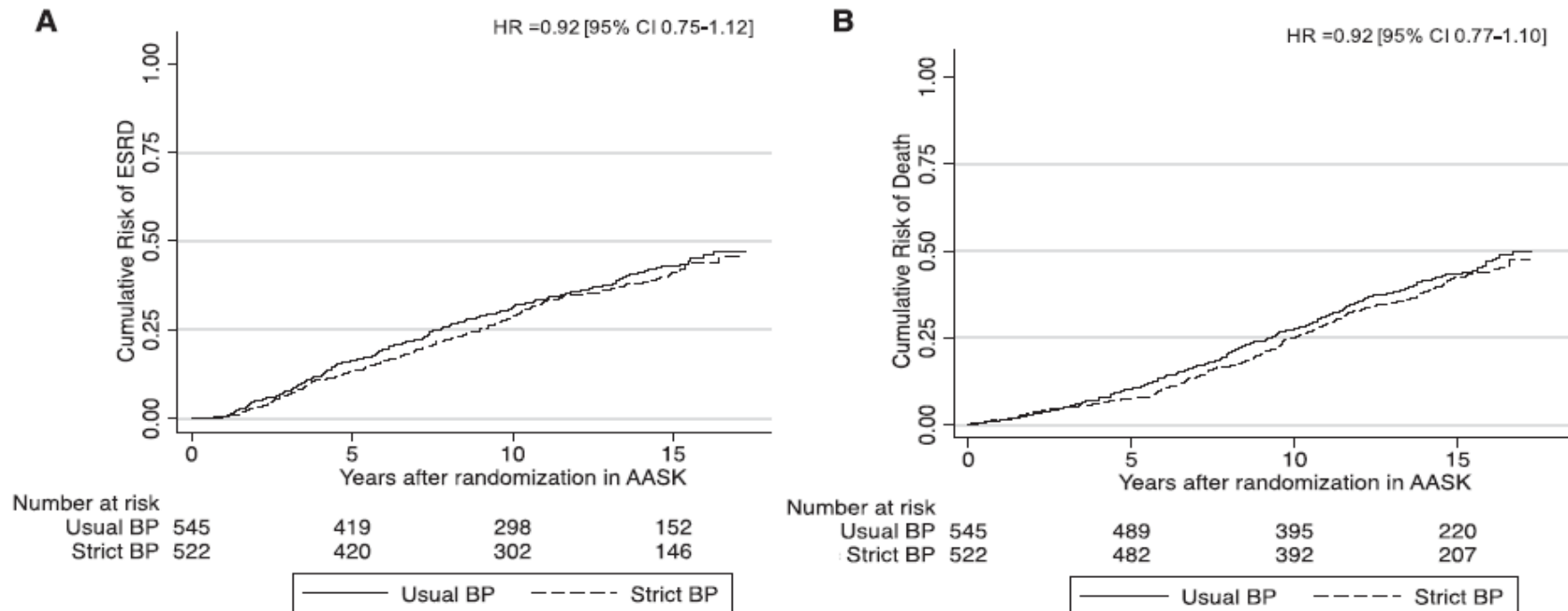


# Management of HTN: Goal and Target

## Design and results of the HOPE-3 and SPRINT trials

	HOPE-3	SPRINT
<b>Intervention</b>	Candesartan/HCTZ 16/12.5 mg versus placebo	Systolic BP target < 120 versus < 140 mm Hg
<b>Specified BP measure</b>	Attended automated BP measurement; average of 2 seated measures at least 1 min apart	Unattended automated BP measurement; average of 3 seated measures 5 min apart
<b>Achieved BP difference</b>	6 mm Hg	13 mm Hg
<b>Follow-up</b>	5.6 yr	3.3 yr
<b>Primary outcome</b>	(i) Composite of cardiovascular death, nonfatal MI, and nonfatal stroke (ii) Composite of the above plus resuscitated cardiac arrest, heart failure, or revascularization	Composite of cardiovascular death, nonfatal MI or acute coronary syndrome, nonfatal stroke, or decompensated heart failure
<b>Event rate</b>	(i) Cumulative incidence 4.1% versus 4.4% (ii) Cumulative incidence 4.9% versus 5.2%	Annual incidence 1.65% versus 2.19%
<b>Treatment effect</b>	(i) HR 0.93; 95% CI, 0.79–1.10 (ii) HR 0.95; 95% CI 0.81–1.11	HR 0.75; 95% CI 0.64–0.89

# Management of HTN: Goal and Target



**BP Control and Long-Term Risk of ESRD and Mortality**

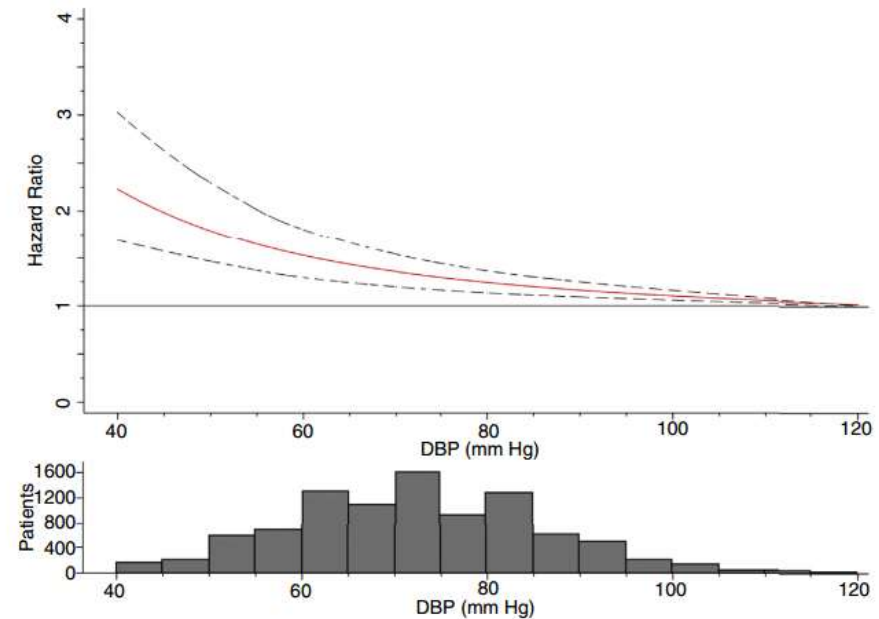
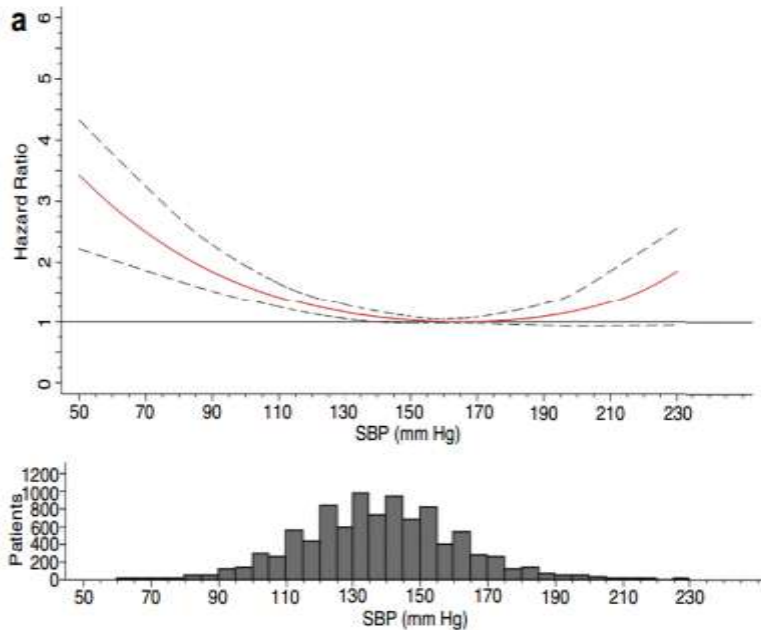
# Management of HTN: Goal and Target



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clinical investigation

www.kidney-international.org

## Multiphasic effects of blood pressure on survival in hemodialysis patients



Thierry Hannedouche<sup>1</sup>, Hubert Roth<sup>2</sup>, Thierry Krummel<sup>1</sup>, Gérard M. London<sup>3</sup>, Guillaume Jean<sup>4</sup>, Jean-Louis Bouchet<sup>5</sup>, Tilman B. Drüeke<sup>6</sup> and Denis Fouque<sup>7</sup>; on behalf of the French Observatory<sup>1</sup>

<sup>1</sup>Service de Néphrologie, Hôpitaux Universitaires de Strasbourg, Faculté de Médecine, Strasbourg, France; <sup>2</sup>Centre de Recherche en Nutrition Humaine Rhône-Alpes, Pôle Recherche CHU-Grenoble, Inserm U1055-Bioénergétique, Université Grenoble-Alpes, France; <sup>3</sup>Hôpital Marqués, Ikeri-Miragis, France; <sup>4</sup>Centre de Rein Artificiel, Taish-La-Demi-Lune, France; <sup>5</sup>Centre de Traitement des Maladies Rénales Saint-Augustin, Bordeaux, France; <sup>6</sup>Inserm U1018, Centre de recherche en Épidémiologie et Santé des Populations, Université Paris-Saclay, Université Paris-Sud, Université de Versailles Saint-Quentin-en-Yvelines, Villejuif, France; and <sup>7</sup>Department of Nephrology, Hôpital Lyon Sud, Université de Lyon, Centre Européen de Nutrition pour la Santé, Lyon, France

Kidney International (Sep 2016) 90, 674–684

**ING**  
Deutsche Bank Group  
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Guideline for the diagnosis and management of hypertension in adults 2016



# Corners

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# Transporters in Focus: What is Pendrin?

EDITORIAL

www.jasn.org

## Pendrin—A New Target for Diuretic Therapy?

Carsten A. Wagner

National Center for Competence in Research Kidney  
of Physiology, University of Zurich, Zurich, Switzerland

BASIC RESEARCH

www.jasn.org

### Double Knockout of the $\text{Na}^+$ -Driven $\text{Cl}^-/\text{HCO}_3^-$ Exchanger and $\text{Na}^+/\text{Cl}^-$ Cotransporter Induces Hypokalemia and Volume Depletion

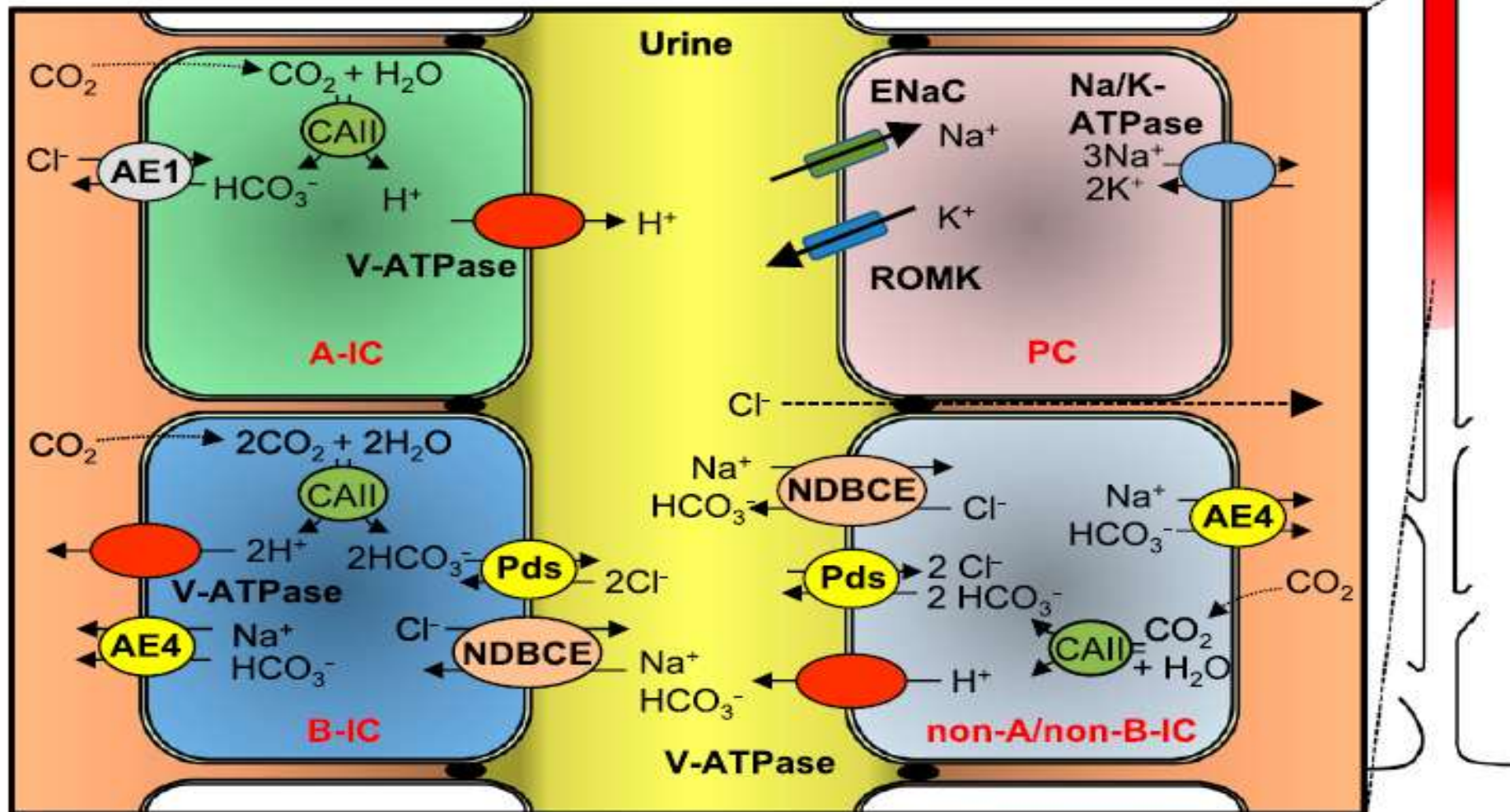
Anne Sinning,<sup>\*</sup> Nikita Radionov,<sup>†‡</sup> Francesco Trepiccone,<sup>†‡</sup> Karen I. López-Cayuqueo,<sup>†‡§</sup>  
Maximilien Jayat,<sup>†‡</sup> Stéphanie Baron,<sup>||</sup> Nicolas Cornière,<sup>||</sup> R. Todd Alexander,<sup>\*\*</sup>  
Juliette Hadchouel,<sup>†‡</sup> Dominique Eladari,<sup>†‡||</sup> Christian A. Hübner,<sup>\*</sup> and Régine Chambrey<sup>†‡††</sup>

<sup>\*</sup>Institut für Humangenetik, University Hospital Jena, Friedrich Schiller Universität, Jena, Germany; <sup>†</sup>Institut National de la Santé et de la Recherche Médicale U970, Paris Cardiovascular Research Center, Paris, France; <sup>‡</sup>Faculty de Médecine, Université Paris-Descartes, Paris, France; <sup>§</sup>Centro de Estudios Científicos (CECs), Valdivia, Chile; <sup>||</sup>Department de Physiologie, Hôpital Européen Georges Pompidou, Assistance Publique-Hôpitaux de Paris, Paris, France; <sup>¶</sup>Service de Néphrologie et Transplantation Rénale, Centre Hospitalier Universitaire de La Réunion, St. Denis, France; <sup>\*\*</sup>Departments of Pediatrics and Physiology, University of Alberta, Edmonton, Alberta, Canada; and <sup>†††</sup>Centre National de la Recherche Scientifique, Paris, France

J Am Soc Nephrol 2016, in press

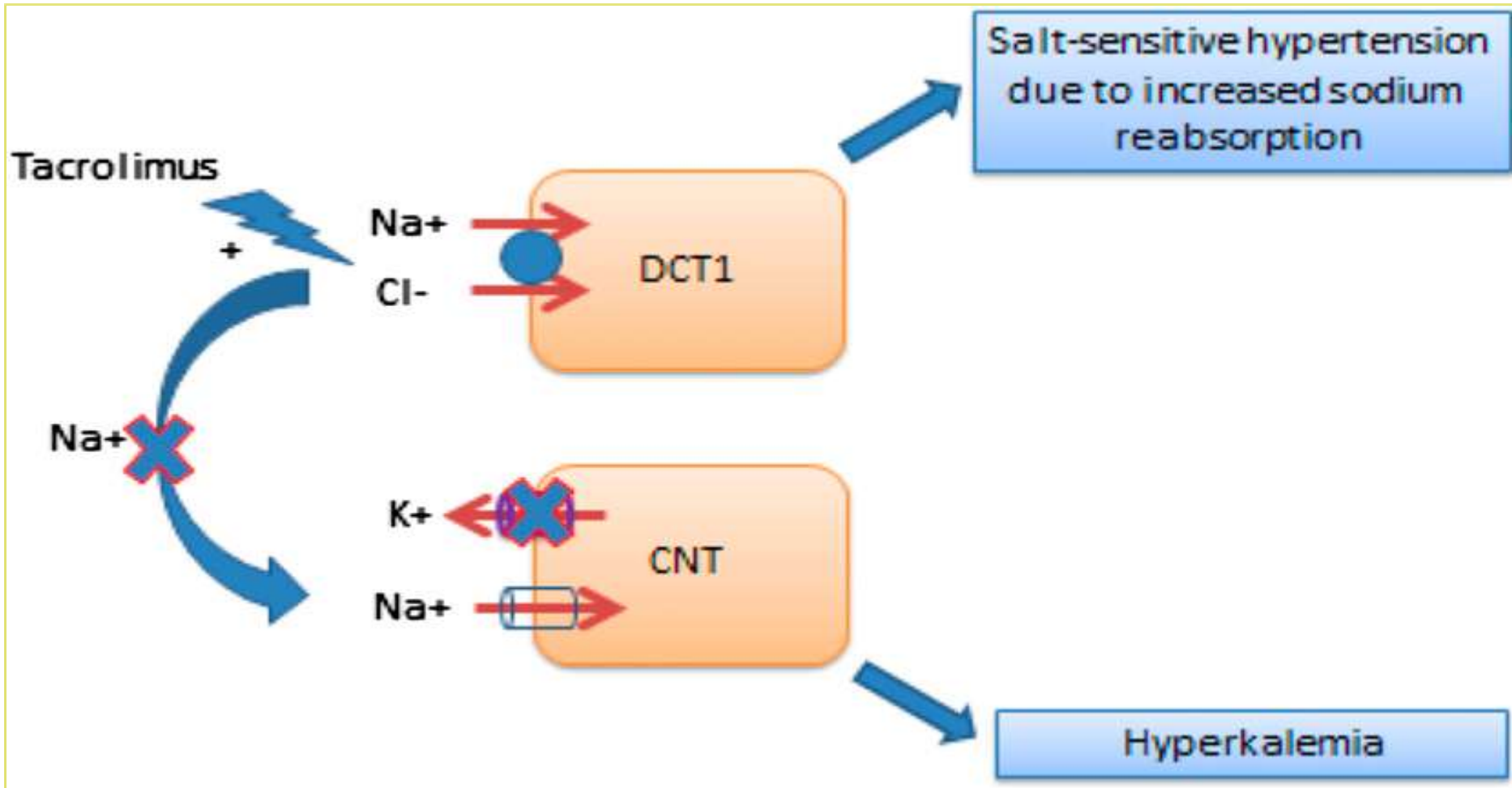
# Transporters in Focus: Where is Pendrin

J Am Soc Nephrol 2016, in press





# Transporters in Focus: Tacrolimus induced HTN?



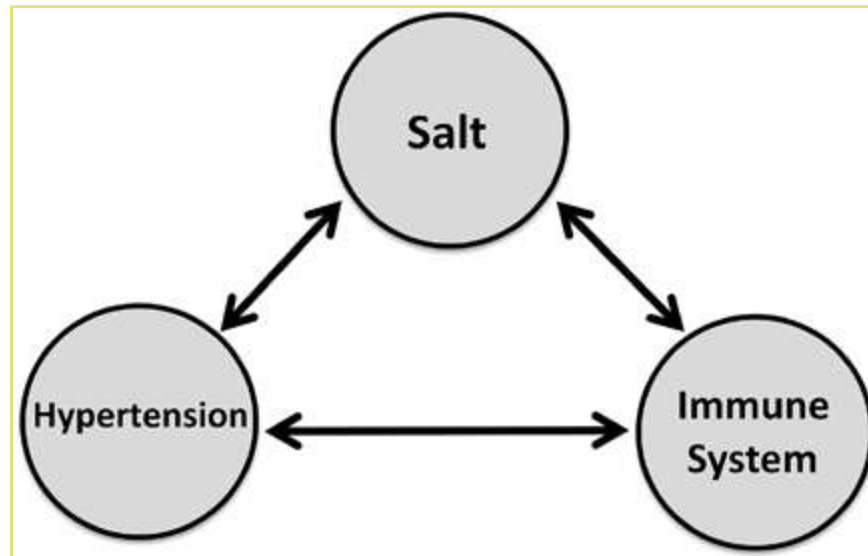
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# Salt and Hypertension

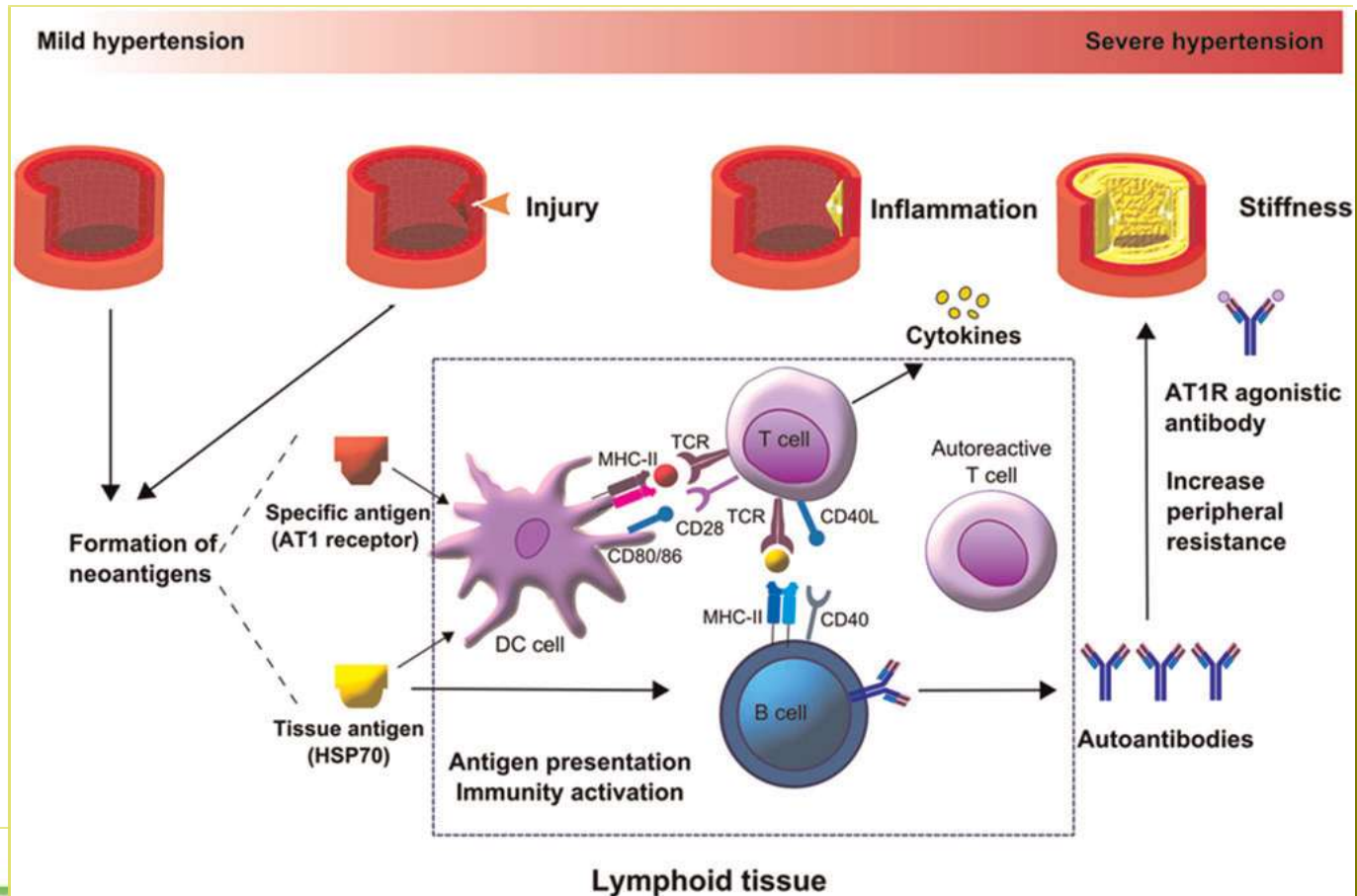
## National Heart, Lung, and Blood Institute Working Group Report on Salt in Human Health and Sickness Building on the Current Scientific Evidence

Young S. Oh, Lawrence J. Appel, Zorina S. Galis, David A. Hafler, Jiang He, Amanda L. Hernandez, Bina Joe, S. Ananth Karumanchi, Christine Maric-Bilkan, David Mattson, Nehal N. Mehta, Gwendolyn Randolph, Michael Ryan, Kathryn Sandberg, Jens Titze, Eser Tolunay, Glenn M. Toney, David G. Harrison



***Hypertension. 2016;68:281-288***

# Hypertension and Immunity



Full Reviews

Immunity in arterial hypertension: associations or causalities?

Hans-Joachim Anders<sup>1</sup>, Marcus Baumann<sup>2</sup>, Giovanni Tripepi<sup>3</sup> and Francesca Mallamaci<sup>4</sup>

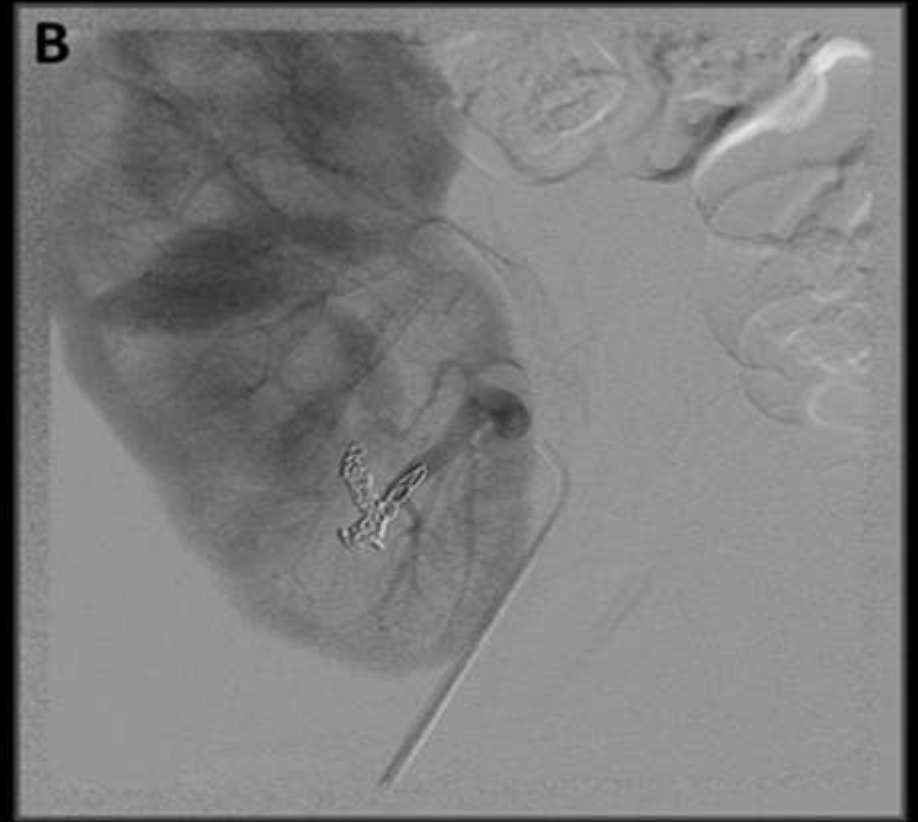
<sup>1</sup>Nephrologisches Zentrum, Medizinische Klinik und Poliklinik IV, Klinikum der Universität München, Munich, Germany; <sup>2</sup>Department of Nephrology, Klinikum rechts der Isar der Technischen Universität München, Munich, Germany and <sup>3</sup>Nephrology, Dialysis and Transplantation Unit & CNR-IRC, Clinical Epidemiology and Physiopathology of Renal Disease and Hypertension of Reggio Calabria, Reggio Calabria, Italy

Nephrol Dial Transplant (2015) 30: 1959–1964

# Post-transplant Hypertension: Mechanisms

Immunosuppressive Agent	Strategy
Steroid	Minimize Dose Elimination
Cyclosporine	Reduce target level Convert to tacrolimus Convert to belatacept
Tacrolimus	Reduce target level Convert to belatacept
Sirolimus/everolimus with CI	Convert to Mycophenolate Eliminate mTORi

# Kidney Transplant and Sudden HTN





# Does Severe HTN Preclude Transplantation

Clinical Transplantation

Kidney transplantation in patients with severe preoperative hypertension

Clin Transplant 2015; 29: 781–785



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# Obesity and Hypertension: Dipping or Non

	Non-dipping				PR	95% CI
	Yes	%	No	%		
Lean <sup>a</sup>	22	13.7	139	86.3	1.00	Ref
Obese <sup>a</sup>	85	34.4	162	65.6	2.15	1.25–3.42

Abbreviation: CI, confidence interval; PR, prevalence ratio.

<sup>a</sup>Lean group defined as 15th–85th BMI percentile, obese group defined as ≥95th BMI percentile.

# Hypertension and Sleep Disorders



Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

Advances in Medical Sciences

journal homepage: [www.elsevier.com/locate/advms](http://www.elsevier.com/locate/advms)



Original Research Article

Assessment of sleep disorders among patients with hypertension and coexisting metabolic syndrome



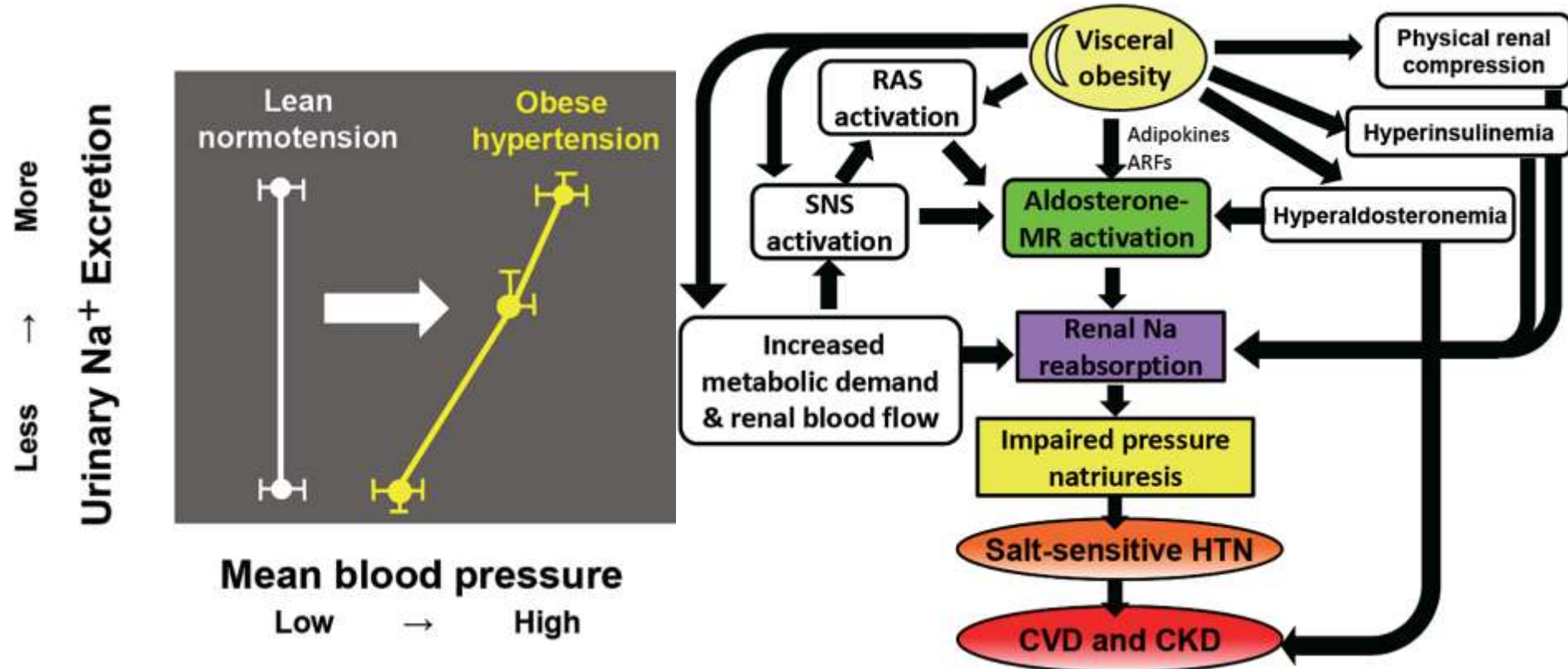
Grzegorz Kielbasa<sup>a</sup>, Katarzyna Stolarz-Skrzypek<sup>b,\*</sup>, Artur Pawlik<sup>a</sup>, Monika Łątka<sup>a</sup>, Tomasz Drożdż<sup>a</sup>, Marta Olszewska<sup>a</sup>, Agata Franczyk<sup>c</sup>, Danuta Czarnecka<sup>b</sup>

<sup>a</sup> Cardiology Student Interest Group, First Department of Cardiology, Interventional Electrophysiology and Hypertension, Jagiellonian University Medical College, Cracow, Poland

<sup>b</sup> First Department of Cardiology, Interventional Electrophysiology and Hypertension, Jagiellonian University Medical College, Cracow, Poland

<sup>c</sup> Department of Clinical Pharmacy, Jagiellonian University Medical College, Cracow, Poland

# Obesity and HTN



# Obesity and Hypertension: Water Aerobics

## Research Article

Water aerobics is followed by short-time and immediate systolic blood pressure reduction in overweight and obese hypertensive women



CrossMark

Raphael Martins Cunha, MSc<sup>a</sup>, Gisela Arsa<sup>b</sup>, Eduardo Borba Neves<sup>c</sup>,  
Lorena Curado Lopes, MSc<sup>d</sup>, Fabio Santana<sup>d</sup>, Marcelo Vasconcelos Noletto<sup>d</sup>,  
Thais I. Rolim<sup>d</sup>, and Alexandre Machado Lehnem, PhD<sup>a,\*</sup>

<sup>a</sup>*Institute of Cardiology/University Foundation of Cardiology, Rio Grande do Sul, Brazil;*

<sup>b</sup>*Faculty of Physical Education, Federal University of Mato Grosso, Mato Grosso, Brazil;*

<sup>c</sup>*Brazilian Army Research Institute of Physical Fitness, Rio de Janeiro, Brazil; and*

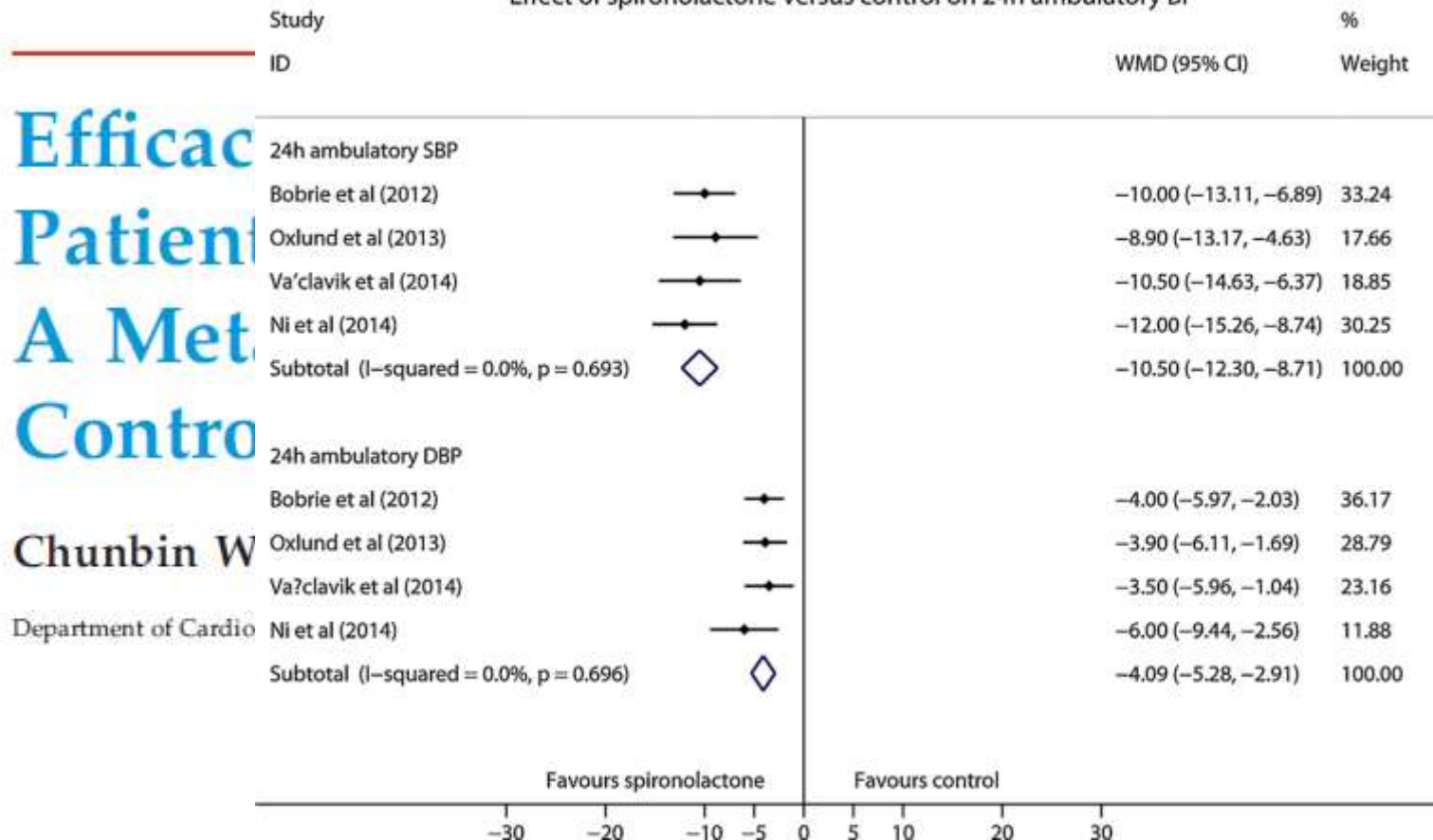
<sup>d</sup>*Exercise Physiology Laboratory, State University of Goiás, Goiás, Brazil*

Manuscript received December 1, 2015 and accepted May 3, 2016



# Resistant Hypertension: Spironolactone Story

Effect of spironolactone versus control on 24h ambulatory BP



Heart, Lung and Circulation (2016), in press

# What is ARNi?

## ARTICLE IN PRESS

IJCA-22711; No of Pages 5

International Journal of Cardiology xxx (2016) xxx–xxx



Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: [www.elsevier.com/locate/ijcard](http://www.elsevier.com/locate/ijcard)



### Review

Angiotensin receptor–neprilysin inhibitor (ARNi): Clinical studies on a new class of drugs

Mauro Gori <sup>a</sup>, Maurizio Volterrani <sup>b</sup>, Massimo Piepoli <sup>c</sup>, Michele Senni <sup>a,\*</sup>

<sup>a</sup> Cardiology, Heart Failure and Heart Transplant Unit, Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy

<sup>b</sup> Cardiology Department, Istituto di Ricovero e Cura a Carattere Scientifico San Raffaele Pisana, Rome, Italy

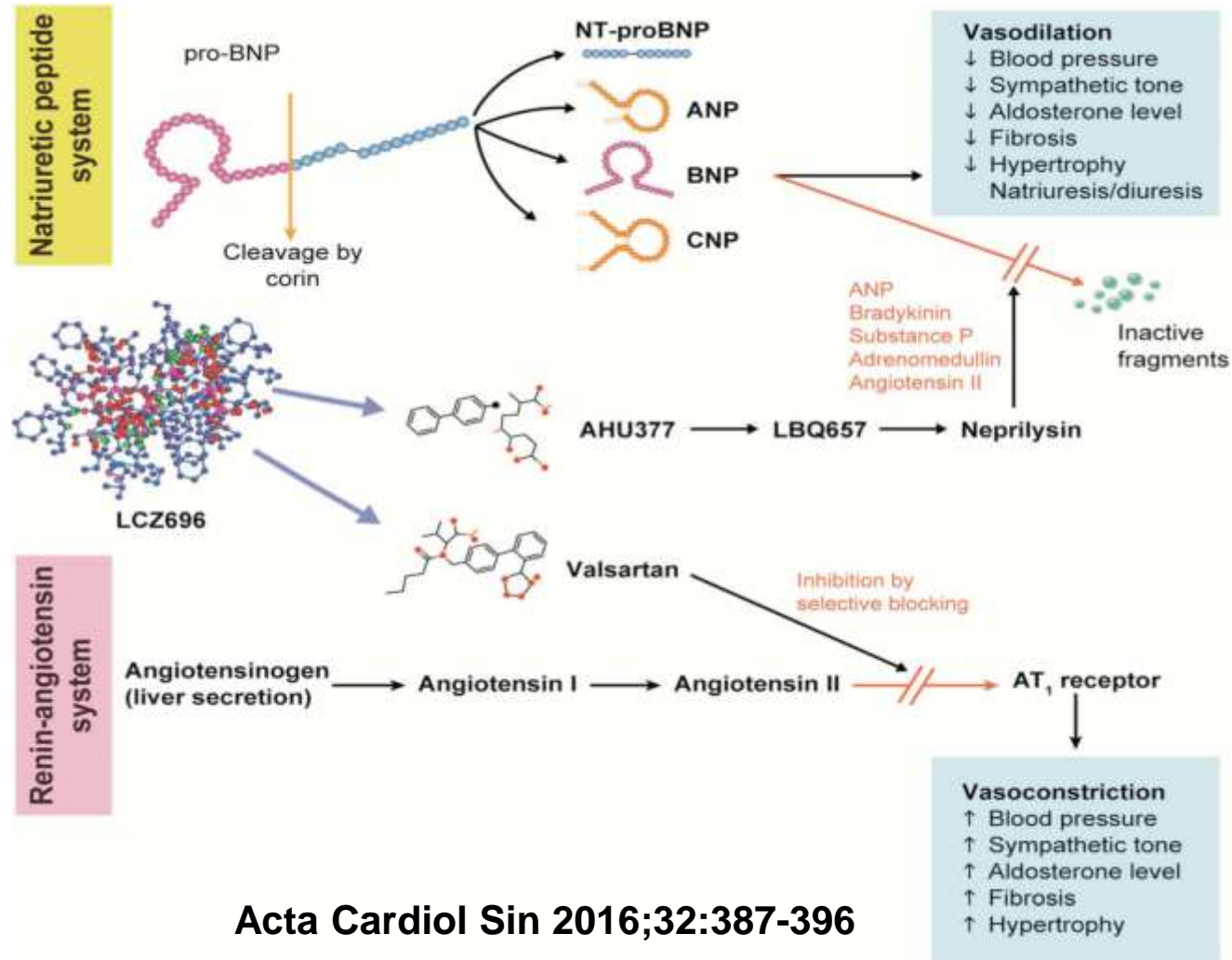
<sup>c</sup> Heart Failure Unit, Cardiology Dept., Guglielmo da Saliceto Hospital, Piacenza, Italy

## LCZ696 (Valsartan/Sacubitril)



# What is ARNi?

## LCZ696 (Valsartan/Sacubitril)



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# Hypertension and Pregnancy



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Drug	Main features with respect to side effects in CKD	FDA “classic” labeling
To be avoided		
Short-acting nifedipine	Contraindicated by the FDA, RCOG, and AIPE due to the risk of severe hypotension with detrimental effects on placental flows. Severe sudden hypotension may have detrimental effects on kidney function	D
ACEi ARBs	Contraindicated due to the risk of major malformations, including cardiovascular, central nervous system, renal, and bone. These drugs are often implicated in AKI, and this may be particularly relevant in pregnant CKD patients	C 1st D 2nd 3rd

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# Medication Adherence

## Brief Review

**Evaluation of Adherence Should Become an Integral Part of Assessment of Patients With Apparently Treatment-Resistant Hypertension**

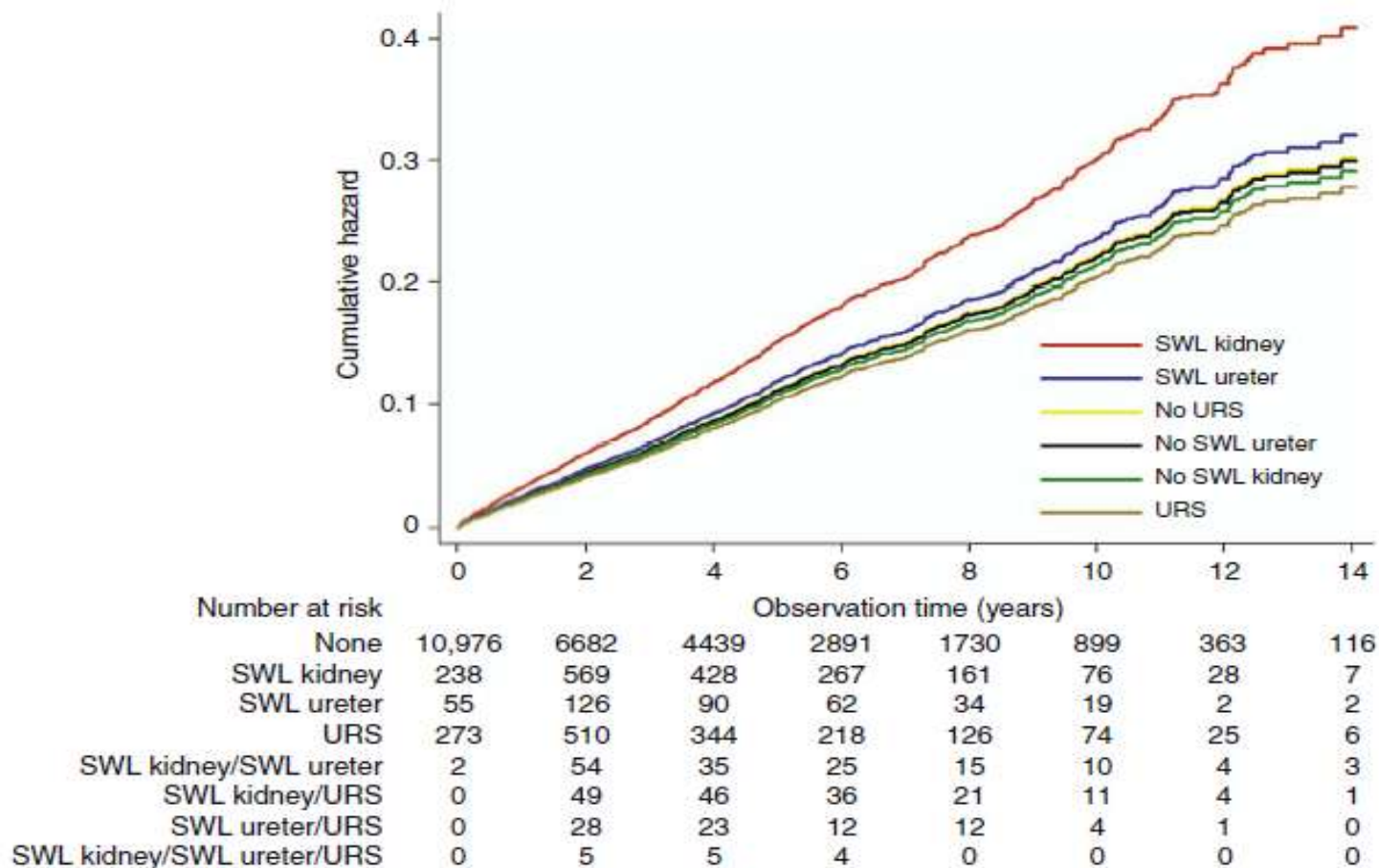
Advantages and Disadvantages		Indirect Methods				Direct Methods			
		Assessment by Clinician	Questionnaires	Pill Count	Prescription Refill	Witnessed Drug Intake	Electronic Monitoring	Tele-Monitoring	Drugs Dosage in Body Fluids
Advantages	Objectivity	↓↓↓↓	↓↓↓	↓↓	↓↓↓	↑↑↑↑	↑↑	↑↑	↑↑↑
	Accuracy	↓↓↓↓	↓↓↓	↓↓	↓↓↓	↑↑↑↑	↑↑↑	↑↑	↑↑↑
	Feasibility	↑↑↑↑	↑↑↑↑	↑↑↑	↑	↓↓↓	↑	↓↓	↓
	Educational value	↓↓↓	↑↑	↑	–	↑	↑↑↑↑	↑↑↑	↑↑
Disadvantages	Cost/workload	↓↓↓↓	↓↓↓	↓↓↓	↑	↑↑	↑↑↑	↑↑↑↑	↑↑
	White coat effect	–	–	↑↑↑	–	–	↓↓↓	↑↑	↑↑↑
	Social desirability bias	↓↓↓↓	↑↑↑↑	↑↑↑	↑↑	–	↑↑	↑↑↑	↓↓
	Manipulability	↓↓↓↓	↑↑	↑↑↑↑	↑↑↑	↓↓↓↓	↑↑↑↑	↓↓	↓↓↓

Social desirability bias: people respond to questioning in ways that make them seem more appealing to others or to healthcare providers. Manipulability: patients willingly manipulate the results of the assessment.

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# Hypertension and ESWL





# Renin Angiotensin Converting Enzyme: ACE-2

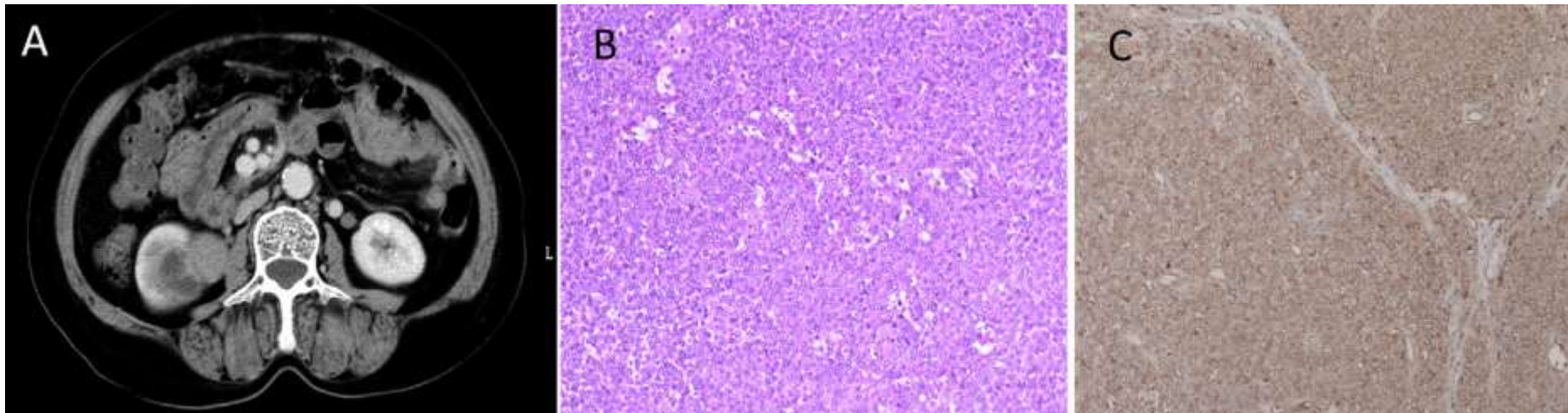
## Renin–Angiotensin System

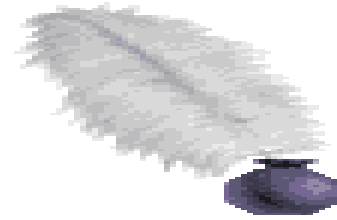
### Angiotensin-Converting Enzyme 2 Metabolizes and Partially Inactivates Pyr-Apelin-13 and Apelin-17 Physiological Effects in the Cardiovascular System

Wang Wang, Shaun M.K. McKinnie, Maikel Farhan, Manish Paul, Tyler McDonald,  
Brent McLean, Catherine Llorens-Cortes, Saugata Hazra, Allan G. Murray, John C. Vederas,  
Gavin Y. Oudit

*Hypertension August 2016;68:365-377*

# Hypertension Case and Messages





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Department of Nephrology  
وحدة أمراض الكلى والكلى

امرض على حفظ القلوب من الأذى  
فرجوعها بعد التنافر يصعبُ

ان القلوبَ إذا تنافر ودُّها  
مثل الزُّجاجة كسرُها لا يُشعبُ